

Remarks

Claims 1, 7, 14, and 19-24 are pending in this application. Claims 26-60 were earlier withdrawn from consideration as drawn to non-elected subject matter and were canceled for the same reason. In addition, claims 2, 13, 18, and 25 were previously canceled, and claims 4-6, 8-12, and 15-17 are canceled herein. Claim 1 has been amended, wherein the subject matter of claims 3, 10, 11, and 15-17 has been incorporated into claim 1. In addition to the amendments to claim 1, claims 7 and 19-24 have also amended. No new matter has been added to the application by virtue of these amendments.

I. Response to Rejections under 35 U.S.C. § 103

A. Legal Standards for Examination under Section 103

The legal standards for examination under 35 U.S.C. § 103 were reviewed in the response to the previous Office Action. That review is hereby incorporated by reference.

The Office Action cited *In re McLaughlin*, 443 F.2d 1392, 170 U.S.P.Q. 209 (C.C.P.A. 1971), as standing for the proposition that hindsight reasoning in making a judgment on obviousness is permissible so long as the hindsight reasoning takes into account only knowledge within the level of ordinary skill in the art at the time the invention was made and does not include knowledge gleaned only from the applicant's disclosure. In the first place, *McLaughlin* was a case where the appellant argued that references

had been improperly combined to attempt to establish a *prima facie* case of obviousness. The court found that there was sufficient motivation in the prior art to make the combination of references. In *dictum* the court made the statement that the Office Action referred to about hindsight. Therefore, *McLaughlin* is *dictum* for the purpose for which the Office Action cited it, and therefore is not binding in subsequent cases, including the instant application. In the second place, a few years later the C.C.P.A. stated in *In re Carroll*, 202 U.S.P.Q. 571, 572 (C.C.P.A. 1979):

One of the more difficult aspects of resolving questions of non-obviousness is the necessity "to guard against slipping into use of hindsight." *Graham v. John Deere Co.*, 383 U.S. 1, 36, 148 USPQ 459, 474 (1965). Many inventions may seem obvious to everyone after they have been made. However, 35 USC 103 instructs us to inquire into whether the claimed invention "would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains." Thus, in deciding the issue of obviousness, we must look at the prior art presented from a vantage point in time prior to when the invention was made, and through the eyes of a hypothetical person of ordinary skill in the art.

Moreover, it has been widely recognized that virtually every invention is a combination of elements and that most, if not all, of these will be found somewhere in an examination of the prior art. This reasoning led the Federal Circuit, in *Connell v. Sears, Roebuck & Co.*, 220 U.S.P.Q. 193, 199 (Fed. Cir. 1983) to state:

The test is whether the claimed invention as a whole, in light of all the teachings of the references in their entirety, would have been obvious to one of ordinary skill in the art at the time the invention was made.

Still further, the Federal Circuit stated as follows:

It is essential that "the decisionmaker forget what he or she has been taught at trial about the claimed invention and cast the mind back to the time the invention was made . . . to occupy the mind of one skilled in the art who is presented only with the references, and who is normally guided by the then-accepted wisdom in the art." [*W.L. Gore*, 721 F.2d at 1553, 220 USPQ at 312-13.] One cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention.

In re Fine, 837 F.2d 1071, 5 USPQ2d 1596, 1599-1600 (Fed. Cir. 1988).

B. Factual and Legal Arguments

1. Claims 1, 3-12, 14-17, and 19-24

Claims 1, 3-12, 14-17, and 19-24 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over U.S. Patent No. 6,743,436 ("Lee") in view of U.S. Patent No. 6,383,471 ("Chen").

It should be recognized that claim 1, as amended, is directed to an injectable anesthetic composition *consisting essentially of* the stated ingredients. "Consisting essentially of" is a term of art that covers combinations with some additional elements, but excludes "additional unspecified ingredients which would affect the basic and novel characteristics of the product defined in the balance of the claim." *Atlas Powder Co. v. E.I. du Pont de Nemours & Co.*, 224 U.S.P.Q. 409, 412 (Fed. Cir. 1984); Donald S. Chisum, 2 Patents § 8.06[1][b] (1995).

Lee discloses an anesthetic microemulsion composition for intravenous injection, which requires as essential ingredients propofol and a poloxamer as a surfactant, alone or in combination with another co-surfactant. (Col. 4, lines 17-19 and 49-52.) Co-surfactants consist of Solutol HS 15, egg lecithin, Labrasol, polyoxy 10 oleyl ether, Tween, ethanol, and polyethylene glycol. (Col. 4, lines 35-42.)

Chen discloses a pharmaceutical composition requiring as essential ingredients an ionizable hydrophobic therapeutic agent and a carrier. (Col. 2, lines 60-62; Abstr.) The carrier must contain a surfactant and an ionizing agent to ionize, and thus solubilize, the therapeutic agent. (Col. 2, lines 62-64; Abstr.) Optionally, the carrier also includes solubilizers, triglycerides, and neutralizing agents. (Col. 2, lines 64-65; Abstr.) The pharmaceutical composition is primarily designed for use in oral dosage forms (Col. 4, lines 62-64; Abstr.), although other dosage forms are not excluded (Col. 35, lines 9-23.) Propofol was included in a long (more than 4 columns) list of ionizable therapeutic agents (Col. 6, line 14, to col. 10, line 35). Ionizing agents are disclosed as pharmaceutically acceptable acids or bases (Col. 11, lines 2-6.) Surfactants are disclosed as hydrophilic, hydrophobic, or a mixture of hydrophilic and hydrophobic surfactants. (Col. 13, lines 62-64.) Specific types and examples of surfactants are disclosed in long (16 columns)

lists at col. 15, line 7, to col. 31, line 25.) Long lists of solubilizers and triglycerides are disclosed, as well. (Col. 31, line 40, to col. 34, line 45.)

The combination of Lee and Chen fails to disclose each and every element of the presently claimed invention, because the combination of Lee and Chen requires a poloxamer as an essential ingredient. Claim 1 excludes a poloxamer as a surfactant, because the surfactant of claim 1, as amended, consists of a bile salt and lecithin. In other words, any additional surfactant is outside the scope of claim 1. Further, a poloxamer would affect the basic and novel characteristics of the product defined in the balance of the claim. Therefore, the combination of Lee and Chen fails to establish a *prima facie* case of obviousness with respect to claim 1 or any claim dependent on claim 1.

The Office Action alleged that it would have been obvious to combine the teachings of Lee and Chen to arrive at the presently claimed invention. Since Lee is drawn to making an injectable composition, and Chen is particularly directed to making an oral formulation, it is not at all clear that a person of ordinary skill in the art would combine these references or what the result would be if these teachings were combined. Further, Applicant could find no mention in these cited references of an object to formulate a clear composition or a disclosure of how to formulate a clear injectable composition. Therefore, the combination of Lee and Chen

would not lead a person of ordinary skill in the art to make a clear, injectable composition. Moreover, Applicant respectfully submits the only mention of optical clarity of the presently claimed invention is found in Applicant's disclosure. The Office Action admitted that neither Lee nor Chen discloses optical clarity. Still further, the solubilizers of Chen's disclosure are optionally added to the combination of an ionizable hydrophobic therapeutic agent, an ionizing agent (which is added to solubilize the therapeutic agent by adjusting the pH of the solution to ionize the therapeutic agent; Col. 1, lines 40-43), and a surfactant to "enhance the solubility of the ionizable hydrophobic therapeutic agent in the carrier system (Col. 31, lines 40-43). Therefore, with respect to claim 1, the Office Action alleges that one would be motivated to select propofol and solutol HS 15 from Lee and to select tetrahydrofurfuryl alcohol polyethylene glycol ether ("glycofurol") from Chen, while ignoring the requirement for a poloxamer from Lee and the requirement for an ionizing agent and a surfactant from Chen. The Office Action also appears to suggest that one would be motivated to make the necessary combination while ignoring the hundreds of other therapeutic agents, ionizing agents, surfactants, solubilizers, and triglycerides disclosed by Chen. The Office Action further suggests that one would be motivated to make a clear injectable composition by combining disclosures that do not mention optical clarity. The Office Action still further

states that one would be motivated to combine an injectable composition with an oral composition to result in a clear microemulsion-containing composition. Applicant respectfully submits that it would not be obvious to a person of ordinary skill in the art to make the presently claimed composition from a combination of Lee and Chen. It would simply be too hypothetical to pick and choose ingredients, as proposed in the Office Action, to result in an optically clear microemulsion composition with a reasonable likelihood of success. Thus, a *prima facie* case of obviousness has not been established.

With all due respect, although the suggestion to combine references may flow from the nature of the problem, "[d]efining the problem in terms of its solution reveals improper hindsight in the selection of the prior art relevant to obviousness." *Monarch Knitting Machine Corp. v. Sulzer Morat GmbH*, 139 F.3d 877, 880, 4 U.S.P.Q.2d 1977, 1981 (Fed. Cir. 1998). Applicant respectfully submits that if one follows the above guidelines and analyzes the art properly, then it would not be obvious to make the invention as claimed.

Still further, references must be considered as a whole, including subject matter that teaches away from the invention as well as subject matter that suggests the invention, and not for their isolated teachings. *Ashland Oil, Inc. v. Delta Resins & Refractories, Inc.*, 227 U.S.P.Q. 657, 669 (Fed. Cir. 1985). Lee

teaches making an injectable composition that requires a combination of propofol and a poloxamer. Therefore, Lee teaches away from making a composition that lacks a poloxamer. Further, Chen teaches making an oral composition containing as essential ingredients an ionizable hydrophobic therapeutic agent (propofol is one of scores of such agents), an ionizing agent, and a surfactant. Optionally, a solubilizer (glycofurol is one of scores of such solubilizers), a triglyceride, and a neutralizing agent can also be included. Therefore, Chen teaches away from making a composition that contains glycofurol without also containing an ionizing agent and a surfactant and also ignores the option of adding a triglyceride and a neutralizing agent. Therefore, Applicant respectfully submits that the Office Action did not consider the cited references in their entirety, and the disclosures of the cited references that teach away from making the presently claimed invention were not given due consideration. For these reasons, a *prima facie* case of obviousness has not been established.

For these reasons, withdrawal of the rejections under Section 103 is respectfully requested.

2. Claims 4-7 and 10-12

Claims 4-7 and 10-12 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Lee and Chen and further in view



of US Patent Application Publication No. 20020107291 ("De Tommaso").

De Tommaso discloses an aqueous, clear, injectable pharmaceutical composition requiring as essential ingredients propofol, a pharmaceutically acceptable salt of a bile acid, and lecithin. (¶ 0005.) The disclosures of Lee and Chen were described above.

The defects in the *prima facie* case of obviousness against claim 1 are also present here. The cited references were not considered in their entirety. It is not clear what combining a microemulsion (Lee), an oral formulation (Chen), and an injectable composition (De Tommaso) would be, but it would not be the presently claimed invention. Also, the cited references were not considered for their disclosures that teach away from making the presently claimed invention, as recited above. The motivation for picking and choosing among the hundreds of disclosed compounds is lacking or found only in Applicant's disclosure. Moreover, it is apparent that the conclusions of the Office Action were arrived at using "hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention," *In re Fine*, 5 USPQ2d 1600, *supra*, which is inappropriate procedure for examining claims under accepted Section 103 jurisprudence. For these reasons, a *prima facie* case of obviousness has not been

established. Withdrawal of the rejections is thus respectfully requested.

3. Failure to Follow *Graham v. John Deere*

*Graham* requires that an analysis under Section 103 include a determination of (1) the scope and content of the prior art, (2) the differences between the prior art and the claimed invention, (3) the level of skill in the art, and (4) the objective evidence of nonobviousness that may have been presented. The first of these two factors were discussed above. It must further be noted, however, that the Office Action failed to make a determination of the level of skill in the art. Since this factor is a required element of Section 103 analysis, the Office Action is flawed. That is, it is impossible to establish a *prima facie* case of obviousness by omitting an essential element of analysis under *Graham*. Since improper procedure was followed, the allegation of obviousness under Section 103 cannot stand. Therefore, withdrawal of the rejection is respectfully requested.

II. Conclusion

Should the Examiner deem it advisable to conduct a telephone interview for any reason, the undersigned attorney would be most agreeable to receiving a telephone call to expedite the prosecution of the application.

For the reasons given above, Applicant respectfully requests reconsideration and allowance of Claims 1, 7, 14, and 19-24 and passage of this application to issue.

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Respectfully submitted,



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